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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,303	04/05/2007	Peter R. Brink	13533/48103	9822

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,303	BRINK ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *8,10-11 and 13-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on August 14, 2009 is acknowledged. Claims 1-34 are pending in this application.

Restriction

1. Applicant's election with traverse of Group I (claims 1-12) and the species of nucleic acid that Cx43 and the corresponding polypeptide encoded by a nucleic acid that encodes Cx43 in the reply filed on August 14, 2009 is acknowledged. The traversal is on the ground(s) that "the claimed method clearly departs from any procedure disclosed by Taheri…the claimed method entails growing a strip of cells in vitro, then implanting the strip of cells in the heart by attaching one end of the strip to healthy tissue in the atrium and attaching the other end to healthy tissue in the ventricle, bypassing the damaged AV node. In contrast, Taheri teaches implanting cells in damaged tissue in the heart and permitting the cells to proliferate outward to establish a connection between the atrium and the ventricles." Applicant further argues that "Pittenger does not compensate for the deficiencies in Taheri". Applicant further argues that "any discussion of a valve is irrelevant to the present invention, which provides an AV bridge, not a valve...Pittenger does not teach producing an atrioventricular bypass tract." Applicant argues that "the claimed bypass bridge is grown in vitro, and then placed into the heart." This is not found persuasive because Taheri et al in view of Pittenger et al teaches the special technical feature of the instant claims. Taheri et al teaches the use of mesenchymal cells treated with connexin and electrically stimulated

in culture to form connections prior to implantation at the AV node. Taheri does not teach culturing the cells into strips. However Pittenger et al teach the method for producing cardiomyocytes in vivo by administering to the heart a cardiomyocyte producing amount of mesenchymal stem cells, and these cells can be solids or semi-solids. Pittenger teaches the use of liquid or matrix, it can be formed into strips that can mimic the size of the ventricular valve, thus would allow ingrowth of the appropriate host cells and renewal of tissue over time. It does not matter whether the implanting the strip of cells in the heart is to healthy tissue in the atrium or to the damaged tissue, since all of the active method steps are taught by Taheri in view of Pittenger. Furthermore, claims 13-23 are drawn to "use of mesenchymal stem cells". As indicated in the previous office action at page 2, "use" claim language is improper under U.S. practice, and has been interpreted as a "method of use". Although Applicant has indicated that these claims have been amended to recite a process rather than a use (see p. 6, 1st paragraph of Applicant's remark), these have not been amended to “method of use.” Applicant indicates that claims 1-7, 9, 11-18, 20, 22-29, 31 and 33-34 read on the elected species.

The requirement is still deemed proper and is therefore made FINAL. Claims 13-34 have been withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 8 and 10 have been withdrawn from further consideration, as being drawn to nonelected species. A search was conducted on the elected species, and prior art was found. Claims 10-11 are also withdrawn from further consideration, as being drawn to

nonelected species. Claims 1-7, 9 and 12 are examined on the merits in this office action.

Rejection

35 U.S.C. 112, 2nd

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 6-7, 9, and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 6 recites, “The method of claim 1, further comprising a step of adding a gene to the mesenchymal stem cells by 35 electroporation.” It is unclear what is meant by “35 electroporation”. It is unclear if 35 electroporation is a name of the device or if it is 35 electroporations or if 35 electroporation is part of a drawing or a figure. The specification has not defined what is meant by “35 electroporation” and there are no figures that refer to “35 electroporation”. Furthermore, it is unclear what is encompassed within the term "gene". Gene encompasses promoters, enhancers, and regulators and other factors, therefore, it is unclear what is encompassed within the term “gene”. Because claims 7, 9 and 11-12 depend from indefinite claim 6 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

35 U.S.C. 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taheri et al (US Patent No. 6,690,970, filed with IDS) in view of Pittenger et al (US Patent No. 6,387,369, filed with IDS).

9. Taheri et al teach a biological pacemaker and implantation catheter for restoring normal or near normal heartbeat function without a mechanical pacemaker. The biological pacemaker is provided by a bridge of implantation cells, that are introduced into an area of electrical malfunction, such as an impaired SA node or a blocked AV node (see abstract). The reference teaches that the implantation cells can be introduced into the malfunction area in any suitable fashion, but are preferably injected via an improved catheter that can be used for both node mapping and cell implantation (see column 3, lines 13-16). implantation cells introducing of about 200 picoamps and 700 picoamps of electricity to SA or AV node cells and this can cause them to dedifferentiate to their original embryonic form (see column 5, lines 1-8). The reference teaches that the implantation cells are either conduction cells obtained from a well-matched homologous AV node (or SA node) donor or autologous cardiac condution cells that have been cultured (see column 5, lines 10-13), meeting the limitation of claim 5. The reference teaches that additional implantation cell options include mixing or transvecting a gene that expresses connexin 43 protein with existing SA or AV node cells (see column 5, lines 23-25), meeting the limitation of claims 3-4, 6 and 9. The reference teaches the use of mesenchymal cells treated with connexin 43 and electrically stimulated in culture (electroporation) to form connections prior to implantation at the AV node (see column 5, lines 43-52), meeting the limitation of claims 1 in part, 3-6, 9. The difference between the reference and the instant claims is that the reference does not teach culturing the cells in strips and suturing.

10. However, Pittenger et al teach a method for producing cardiomyocytes *in vivo* by administering to the heart a cardiomyocyte producing amount of mesenchymal stem cells. These cells can be administered as a liquid injectable or as a preparation of cells in a matrix which is or becomes solid or semi-solid (see abstract). The reference further teaches the use of liquid cell treatment and matrix cell support treatment. The reference teaches that the MSCs are administered in a biocompatible medium which is, or becomes in situ at the site of myocardial damage, a semi-solid or solid matrix. For example, one or more layers of a flexible, solid matrix that is implanted in its final form, such as impregnated fibrous matrices. This in turn, enhances the opportunity for the administered MSCs to proliferate, differentiate and eventually become fully developed cardiomyocytes...they then integrate with the recipient's surrounding myocardium (see column 2, lines 31-34,'38-40, 42-47). The reference teaches that the incision was closed with sutures (see column 6, lines 30-37).

11. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Taheri et al and Pittenger et al, since both teach producing an atrioventricular bypass tract, comprising mesenchymal stem cells. Taheri teaches that the implantation cells can be introduced into the malfunction area in any suitable fashion, but are preferably injected via an improved catheter that can be used for both node mapping and cell implantation. Pittenger teaches that the MSCs are introduced by incision or injection. One of ordinary skill in the art would have been motivated to combine, since Pittenger teach the use of liquid or matrix, therefore, it can be formed into strips that mimic the size of the ventricular valve, thus would allow ingrowth of the

appropriate host cells and renewal of tissue over time (see column 1, lines 28-31). There is a reasonable expectation of success, since both Taheri and Pittenger teach a method for replacing cells *ex vivo* in a heart valve for implantation, and renewal of tissue over time could be achieved.

12. Claims 1-7, 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taheri et al (US Patent No. 6,690,970, filed with IDS) in view of Pittenger et al (US Patent No. 6,387,369, filed with IDS) as applied to claims 1-7 and 9 above, further in view of Donahue et al (US 2002/0155101 A1).

13. The teachings of Taheri et al and Pittenger et al are described, *supra*. The difference between the reference and the instant claims is that the reference does not teach adding alpha and accessory subunits of L-type calcium channel.

14. However, Donahue et al teach methods of treating cardiac arrhythmia (see abstract). The reference teaches that genes that could be used to affect arrhythmias include ion channel and pumps (a-subunits or accessory of the following: potassium channels, sodium channels, calcium channels, chloride channels, stretch-activated cation channels…) or genes for proteins that affect the expression, processing or function processing of these proteins.

Therefore, it would have been obvious to one of ordinary skill in the art to add in genes or accessory subunit that would affect arrhythmias in the atrioventricular bypass tract for a heart. Donahue teaches that genes that could be used to affect arrhythmias include

ion channels and pumps that include α -subunits or accessory of calcium channel. There is a motivation to combine since Taheri et al teach that gene that expresses connexin 43 protein would serve to promote the formation of gap junctions, which are essential for electrical connection to existing myocardial cells (see column 5, lines 23-27), and Donahue teaches that α-subunits or accessory of calcium channel affect cardiac arrhythmias. The MPEP states the following: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious). But see In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987) ("Based upon the prior art and the fact that each of the three components of the composition used in the claimed method is conventionally employed in the art for treating cooling water systems, the board held that it would have been prima facie obvious, within the meaning of 35 U.S.C.

103, to employ these components in combination for their known functions and to optimize the amount of each additive....Appellant argues... hindsight reconstruction or at best,... obvious to try'.... We agree with appellant."). There is a reasonable expectation of success, since connexin is serve to promote the formation of gap junctions, which are essential for electrical connection to existing myocardial cells and α-subunits or accessory of calcium channel affect cardiac arrhythmias, combining the two known for the same purpose would at least have an additive affect.

Conclusion

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654